The Treatment of Psychiatric Disorders with Metrazol

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

The Treatment of Psychiatric Disorders with Metrazol

1935—1960

A SELECTED ANNOTATED BIBLIOGRAPHY

Compiled for the Psychopharmacology Service Center
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By Miriam R. Geller

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FOREWORD

This reference list contains *controlled* studies on the treatment of psychiatric disorders with Metrazol published between the years 1935 and 1960. The annotations which accompany each reference are intended to be factual summaries of the author's methodology and results, and are not evaluative or critical. The list is arranged alphabetically by author, and includes a subject and author index.

The majority of the references are in the area of clinical psychiatry and cover both convulsive and nonconvulsive treatment. Pharmacological, biochemical, and physiological studies were also included when the sample under observation was composed of psychiatric patients.

The 83 references included in this study were selected from 1,030 publications which were examined in detail. However, many more were found not to be available. This was especially true of foreign language papers published during the years of the Second World War. The list, therefore, should not be treated as an exhaustive collection of the world literature.

The following were used as source materials: *Current List of Medical Literature,* July 1956—December 1960; *Excerpta Medica,* Section 8 (Neurology and Psychiatry), 1948–1960; *Psychological Abstracts,* 1936–1960; *Quarterly Cumulative Index Medicus,* January 1935—December 1956.

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MIRIAM R. GELLER

JUNE, 1962

Subject Index

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Author Index

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Bibliography

1. ANDROP, SERGE, AND GREEN, ETHEL. Résumé of Metrazol-shock therapy in schizophrenia. *Diseases of the Nervous System,* 1941, 2, 222–228. (July.)

A group of 82 chronic schizophrenic patients were treated with Metrazol and the results contrasted with those obtained in a group of 212 patients who did not receive shock therapy. Immediately following Metrazol treatment 50% of the patients were found to be improved, but there were no complete remissions. After a followup study from 6 months to 2 years after termination of treatment, only 24% of the patients were found to be improved, indicating a relapse rate of 50%. In the group not receiving shock therapy, 33% of the patients showed improvement. In both the treated and untreated groups those patients whose psychosis was of a shorter duration had the more permanent improvements.

2. BAIN, A. J. The influence of Cardiazol on chronic schizophrenia. *Journal of Mental Science,* 1940, 86, 502–513. (May.)

In a small control series of cases of chronic schizophrenia (9 treated and 9 untreated patients) it was found that immediately following the termination of treatment only 1 treated patient showed any improvement as compared with 1 improved and 1 recovered in the control group. A year later none of the treated and one of the controls was considered improved. The author concludes that in chronic cases of schizophrenia it does not seem justifiable to use Metrazol therapy.

3. BARRABEE, PAUL, WINGATE, JAMES H., PHILLIPS, BERNARD D., AND GREENBLATT, MILTON. Effects of L-glutavite compared with Metrazol and vitamins on aged female psychotic patients. *Postgraduate Medicine,* 1956, 19 (4), 485–491. (April.)

Thirty aged female psychotic patients were divided into three test groups of 10 each. One group received L-glutavite, one Metrazol, and one vitamins for a period of 3 months. Mental and social behavior were evaluated before and after treatment by a revised Barrabee-Hyde Hospital Social Adjustment Scale and a specially prepared mental status scale. The entire sample of 30 patients was found to have post-test changes in ratings in the direction of improvement. However, there were statistically significant differences in the amount of these changes among the three groups. Patients who received L-glutavite showed the most favorable picture, followed by the group that received vitamins, while the group that received Metrazol showed the least improvement. The authors suggest that the improvement noted in the Metrazol group may not have been due to the drug, but to the social program.

4. BARRETT, JOSEPH E., FUNKHOUSER, JAMES B., AND BARKER, W. ALLEN. Spinal injuries in shock and epileptic convulsions. *American Journal of Psychiatry,* 1942, 99, 387–390. (November.)

Twenty Metrazol treated cases, 20 electric shock treated cases, 20 epileptics, and 20 nonconvulsive control cases were selected for study. The criteria for selection were that the patients be approximately of the same age groups, and that all cases, except for the controls, had had major convulsive seizures. A flat lateral plate was made of the dorsal spine in each of the cases. Sixty percent of the males and 30% of the females undergoing Metrazol therapy were found to have verte-

bral fractures. In the electric shock treated series, 30% of the males and none of the females had vertebral fractures. In the epilepsy series, 40% of the males and 50% of the females had vertebral fractures. A high incidence of hypertrophic arthritis was found in all the groups studied.

5. BATEMAN, J. F., AND MICHAEL, NICHOLAS. Pharmacological shock treatment of schizophrenia. A statistical study of results in the Ohio State hospitals. *American Journal of Psychiatry,* 1940, 97, 59–67. (July.)

This is a survey of the results of the treatment of schizophrenic patients with insulin, Metrazol, and insulin and Metrazol combined in all Ohio State hospitals for the years 1937 and 1938. All untreated schizophrenic patients admitted to one of the hospitals between 1934 and 1935 were used as a control group. Four-hundred and sixteen patients (186 males and 230 females) were treated with insulin shock. Of these, 130 (31.2%) recovered, 54 (12.9%) were much improved, 116 (27.8%) were improved, and 115 (27.6%) were unimproved. A total of 579 patients (323 males and 256 females) were treated with Metrazol; 88 (15%) recovered, 72 (12.4%) were much improved, 199 (34.3%) were improved and 218 (37.6%) were unimproved. In 5 of the hospitals, 61 patients (27 males and 34 females) were treated with a combination of insulin and Metrazol; 9 (14.7%) recovered, 10 (16.3%) were much improved, 29 (47.5%) were improved and 13 (21.3%) were unimproved. Out of 325 untreated cases in the control group 49 (15%) recovered, 79 (24.3%) were improved, and 197 (60.6%) were unimproved. Other statistical data included are the outcome of treatment according to hospital, according to age at beginning of treatment, and according to duration of psychosis before treatment.

6. BLAUROCK, MELVIN F., LOW, ABRAHAM A., AND SACHS, MANDEL. Influence of fear, pharmacologic action and convulsion in Metrazol therapy. *Archives of Neurology and Psychiatry,* 1939, 42, 233–236. (August.)

Seventeen patients undergoing a course of Metrazol treatment were used as subjects. Six of the patients, during the second, third or fourth week of treatment were given an injection of Metrazol slowly enough so that a convulsion did not take place. The remaining 11 patients, each on a separate day, were given physiologic saline instead of Metrazol. In each treatment situation the vital signs were registered every 5 minutes during the first half hour after injection, every 10 minutes during the following hour, and every 30 minutes for another 1½ hours. In addition, a sample of blood was collected 10 minutes, 1 hour, and 2 hours respectively, after the injection. The pH and the carbon dioxide, calcium and dextrose contents of the serum were determined, and leucocyte counts were made. Results showed that there were no marked effects on the vital signs nor on the pH and carbon dioxide content of the blood unless a convulsion occurred.

7. BULLEY, K. G., AND GREENE, B. L. Incidence of pulmonary tuberculosis in schizophrenic patients following Metrazol convulsive therapy. *American Journal of the Medical Sciences,* 1941, 201, 504–509. (April); also, *Elgin State Hospital Papers,* 1941, 4, 140–144. (April.)

Of 277 schizophrenic patients who had been previously treated with Metrazol therapy, 25 (8.3%) developed pulmonary tuberculosis as compared with 3% of a similar group of schizophrenics not so treated. The authors conclude that Metrazol therapy should be given in the presence of active pulmonary tuberculosis only when all risks have been considered and when the mental condition is very seriously influencing the physical status of the patient.

8. COHEN, LOUIS H. The therapeutic significance of fear in the Metrazol treatment of schizophrenia. *American Journal of Psychiatry,* 1939, 95, 1349–1357. (May.)

In an effort to evaluate the therapeutic effects of fear induced by treatment with Metrazol the author induced prolonged fear states without seizures in 20 schizophrenic

patients and compared the therapeutic outcome with that of 10 daily convulsive seizures given to the same group of patients. Results showed that the procedure of "induced fear" was of less therapeutic value than that characterized by convulsions. The author concludes from these findings that "fear" is not the active factor in Metrazol therapy.

9. COLOMB, H. O., AND WADSWORTH, G. L. An analysis of results in the Metrazol shock therapy of schizophrenia. *Journal of Nervous and Mental Disease,* 1941, 93, 53–62. (January.)

Of 97 cases of dementia praecox treated with Metrazol 18.4% recovered, and 24.7% were improved. In an untreated control group of 276 patients 10.1% recovered, and 30% were improved. Patients in whom good results were obtained with Metrazol were found to improve with the first five convulsions. Conversely, those who did not improve with the first five were not helped by many.

10. CRAIG, J. B., AND SCHILLING, M. E. A comparison of the results of Metrazol therapy with a group of matched control cases. *American Journal of Psychiatry,* 1941, 98, 180–184. (September.)

Twenty-three patients treated with Metrazol were matched on ten points (diagnosis, age, period of hospitalization, duration of illness before admission, hereditary factors, premorbid personality, premorbid achievement, neuropathic traits, mental status, and chief symptoms) with 23 patients treated by other means. A comparison of results showed that at the time of discharge 1 patient was recovered, and 14 were improved in the Metrazol group as compared with 5 recovered and 9 improved in the group that was treated by other means. On followup one and one half years later 4 of the Metrazol group were recovered and 16 improved, as compared with 5 recovered and 2 improved in the control group. The authors conclude from their findings that patients treated with Metrazol appear to show more consistent gains and seem to be able to adjust better to extra-mural life than do patients treated by other methods.

11. CUMMINS, J. A. Metrazol complications as affected by the use of curare. *Canadian Medical Association Journal,* 1942, 47, 326–329. (October.)

Of 122 patients receiving Metrazol alone 14.8% suffered from compression fractures of the vertebrae as compared with only 3.4% of the 118 patients who were treated with Metrazol plus curare.

12. DEAN, STANLEY ROCHELLE. Studies in convulsant therapy. II. The role of alkalinization. *Journal of Laboratory and Clinical Medicine,* 1938, 24, 256–259. (December.)

Of 636 Metrazol injections, 287 were given in conjunction with an alkaline regime, and 349 were administered to patients who received an ordinary diet without alkalies. No difference was found in the size of the initial convulsant dose, in acquired tolerance, or duration and intensity of the Metrazol episode between the two groups.

13. DEDICHEN, H. H. A comparison of 1,459 shock-treated and 969 non-shock-treated psychoses in Norwegian hospitals. *Acta Psychiatrica et Neurologica,* 1946, Supplement 37, 3–160.

A very detailed analysis is presented of 1,459 shock-treated patients and 969 similar control patients who received no shock treatment. Of the treated patients, 1,087 were given Metrazol, 243 insulin and 129 summation treatment (combined insulin and Metrazol). All patients were divided into three groups by diagnosis: Group I, hebephrenic, paranoid and catatonic syndromes without manic-depressive or confusional trends; Group II, hebephrenic, paranoid or catatonic syndromes with manic-depressive or confusional trends; and Group III, manic-melancholic syndromes. Remission rates for patients in Group I treated with Metrazol were 63.3% for those ill 6 months, 30% for those ill 1 year, 12.3% for those ill 1 to 2 years, and 10.7% for those ill 2 to 5 years. The same rates for Group II patients were 77.4%, 62.8%, 29.5%, and 23.3%. For Group III patients the rates were 81.7%, 75.8%, 33.3%, and 61.1%. In the insulin treated patients

remission rates for Group I were 56% for those ill less than 1 year and 4% for those ill more than 1 year. In Group II the same rates were 62% and 18%, and in Group II 33%, and 43%. For the summation treated patients the remission rates for Group I were 55% for those ill less than 1 year and 11% for those ill more than 1 year. In Group II the same rates were 67% and 16%, and in Group III 100% and 40%. In the control group the remission rates for Group I patients were 14.7% for those ill 6 months; 12.5% for those 6 months to 1 year; 7.9% for those ill 1 to 2 years; and 8.3% for those ill 2 to 5 years. The same rates for Group II patients were 46.9%, 33.3%, 32%, and 29.4%. For Group III patients they were 82%, 75%, 60%, and 33.3%.

14. EASTON, NORMAN L., AND SOMMERS, JOSEPH. Vertebral fractures in Metrazol therapy with and without the use of curare as a supplement. *Journal of Nervous and Mental Disease,* 1944, 99, 256–263. (March.)

In a series of 800 Metrazol treated cases, a fracture incidence of 26.1% was found as compared with a fracture incidence of 5.8% in 275 cases treated with Metrazol plus curare. In the curare treated group there was also a decrease in the degree of the compression and the number of vertebrae involved.

15. FINGERT, HYMAN H., KAGAN, JULIA R., AND SCHILDER, PAUL. The Goodenough test in insulin and Metrazol treatment of schizophrenia. *Journal of General Psychology,* 1939, 21, 349–365. (October.)

Fifty Goodenough drawings were obtained from untreated schizophrenics, and 40 from similar patients treated with insulin or Metrazol shock therapy. Characteristics of untreated schizophrenic drawings were: (1) incompleteness and distortion, (2) disproportion between parts of the body, (3) stereotypy, (4) disruptive addition of primitive form elements, and (5) perseveration. These same characteristics were found in the patients treated with Metrazol and insulin plus signs of organic confusion in gestalt perception and representation. The drawings, before the beginning of treatment and after recovery or improvement showed the same basic pattern; however, the basic schizophrenic pattern was held to less rigidly after treatment was finished. The authors conclude from these findings that the effect of insulin and Metrazol therapy lies not in a direct attack on the schizophrenic structures, but on deeper seated structures, the changes in which may be reflected in the reorganization of the schizophrenic process.

16. FINIEFS, L. A. The results of treatment of a thousand cases of schizophrenia. *Journal of Mental Science,* 1948, 94, 575–580. (July.)

The results of treatment of 1,009 cases of schizophrenia extending over a 17 year period are reported. Of these, 378 were treated with insulin coma, 82 with convulsion therapy (Metrazol and E.C.T.), and 103 with a combination of insulin and convulsions. Comparison is made with an untreated control group of 446 cases. Discharge rates were: 39% for those treated with convulsion therapy, 54.2% for those treated with insulin coma therapy, 54.3% for those treated with a combination of insulin and convulsions, and 34.5% for the untreated controls. The average stay in the hospital for the untreated cases was 8.3 months, as compared with 5 months for the treated cases. A 5 year followup study showed that of 156 nontreated cases 40% were still well, as compared with 62.2% of 188 treated cases. A greater percentage of both acute and chronic cases were discharged who received either insulin coma with convulsions or insulin coma alone than were those treated with convulsions alone.

17. GÄDE, E. B., AND HEINRICH, K. Klinische Behandlungsdauer und Behandlungserfolg bei schizophrenen Psychosen. Ein Vergleich der neuroleptischen Therapie mit den älteren Behandlungsverfahren. (Duration and success of clinical treatment in schizophrenic psychoses. A comparison of neuroleptic treatment with the older methods of treatment.) *Nervenarzt,* 1958, 29, 363–364.

The author compares the results obtained with electro-, insulin-, and Metrazol-shock therapy in 242 cases of schizophrenia with those obtained in 159 cases treated with chlorpromazine and 91 cases treated with a combination of chlorpromazine and shock therapy. It was found that for those patients diagnosed "paranoid hallucinatory" (342 of the total of 492 patients), remissions were obtained several weeks earlier with chlorpromazine than with either shock therapy or a combination of chlorpromazine and shock therapy.

18. GOOD, RANKINE. Anomalous cardiac occurrences during Cardiazol treatment of the psychoses and psychoneuroses. *Journal of Mental Science,* 1940, 86, 260–275. (March.)

In a study to determine whether Metrazol caused abnormalities of the heart, 65 patients were treated with convulsive doses of Metrazol and 10 with subconvulsive doses and the electrocardiograms of the two groups compared. Of the patients treated with convulsive doses, 42 (65%) showed abnormalities of the heart immediately after treatment, whereas only 1 patient treated with subconvulsive doses showed any abnormality. No relationship was found between the occurrence of the abnormalities with such factors as age, sex, stature, state of nutrition, physical health, duration of convulsion, dosage of Metrazol, rate of administration, or depth of cyanosis. Those patients who were available for followup showed no abnormality at any time, either clinically or electrocardiographically. The author concludes that the occurrence of these abnormalities should be regarded as normal responses of the heart muscle to the strain of a convulsion and not as an indication for cessation of treatment.

19. GROSS, MARTIN, AND FINN, MICHAEL H.P. Oral Metrazol therapy in psychotic senile and arteriosclerotic patients. *Journal of the American Geriatrics Society,* 1954, 2, 514–518. (August.)

Oral Metrazol medication was administered to 10 geriatric patients with diagnoses of senile psychosis with cerebral arteriosclerosis. Five patients of approximately the same age and mental condition served as controls and were given placebos which had the same appearance as the Metrazol tablets. A behavior rating scale and a series of psychological tests (the Wechsler Memory Scale, the figure-drawing, the Rorschach, and the Bender-Gestalt tests) were used for evaluating patients. An analysis of the rating scale results for the Metrazol group showed that no patient had improved sufficiently to be discharged and only one improved sufficiently to be transferred to an open ward. Of the control group, one patient was rated as definitely improved. The psychological tests used were found to be insufficiently sensitive for the evaluation of severely senile, disturbed psychotics.

20. HAAS, ADOLF. Pentamethylenetetrazol (Metrazol) in the treatment of the geriatric patient. Evaluation on an open geriatric ward. *Journal of the American Geriatrics Society,* 1960, 8, 625–627. (August.)

Twenty-four hospitalized geriatric patients were selected to study the effect of Metrazol on the mild chronic brain syndrome or chronic psychosis of old age. Fifteen of the patients were given Metrazol in tablet form, 4 in liquid form, and 5 received a liquid placebo tasting like Metrazol. At the end of a 5-week period there was no improvement in either the group receiving Metrazol or in the one receiving a placebo. In a second study, 9 patients received a higher dosage of Metrazol (0.2 gm. as compared with the initial dosage of 0.1 gm.) of which 3 showed definite improvement. Based on his observations the author concludes that Metrazol may cause some improvement in some patients with mild organic brain changes either by increasing oxygenation in the brain or by increased synaptic activity.

21. HARRIS, ARTHUR. Cardiazol treatment of schizophrenia. *Journal of Mental Science,* 1938, 84, 735–775. (September.)

Of 35 cases of schizophrenia treated with Cardiazol, 7 recovered, 10 were improved,

and 2 had temporary remissions. In contrast, of 106 untreated controls, 35 (33%) were sufficiently recovered from their illness to have been discharged. The author's general impression is that Cardiazol therapy does not exercise any profound effect on the course of schizophrenia, but may hasten recovery in cases which are going to remit or prevent the worst ravages in cases which are not going to remit. A lengthy review of the literature is also presented on the pharmacology of Cardiazol, the physiology of convulsions, the technique of treatment, the physiological concomitants of the fit, and Meduna's and alternative hypotheses.

22. HEILBRUNN, GERT, AND LIEBERT, ERICH. Observations on the adrenalin level in the blood serum during insulin hypoglycemia and after Metrazol convulsions. *Endocrinology,* 1939, 25, 354–358. (September.)

An investigation is presented on the adrenalin content of the blood serum during the various phases of insulin hypoglycemia in 25 schizophrenic patients. Control experiments were carried out on the blood serum of schizophrenic patients not receiving any insulin. Three different types of reactions were obtained: (1) patients who went into shock readily and remained in coma until the hypoglycemia was interrupted showed an adequate adrenal response to insulin 90 minutes after the injection; (2) patients who did not seem to be affected clinically by the insulin displayed a marked rise in the adrenalin level of the blood; and (3) patients who did not go into shock rapidly, fluctuated between a wakeful state and deep coma, and displayed severe muscular twitchings and myoclonic movements had an adrenalin output that was found to be dependent upon their muscular movements. This latter finding was confirmed by observation of the adrenalin level in the blood serum after Metrazol convulsions.

23. HEIMAN, MARCEL. On the use of strychnine in the curare-aided Metrazol treatment of psychoses. *American Journal of Psychiatry,* 1943, 99, 706–711. (March.)

A modification of Metrazol treatment is described in which strychnine is given simultaneously with curare intravenously in amounts of 1/120 gr. to 1/130 gr. preceding the injection of Metrazol. Sixteen patients treated in this way were compared with 16 treated without strychnine as an adjuvant. It was found that with the use of strychnine the maximum average dose of Metrazol required was only 23.5% higher than the initial average dose, whereas without strychnine it was 62.7%. The author concludes that strychnine is of value because it sensitizes the central nervous system to Metrazol.

24. HINKO, EDWARD N., AND LIPSCHUTZ, LOUIS S. Five years after shock therapy. A preliminary report. *American Journal of Psychiatry,* 1947, 104, 387–390. (December.)

This study presents the results of 191 patients treated with insulin, 242 with Metrazol, and 24 with electroshock therapy. Comparison is made with a control group of 289 untreated patients matched with regard to age, sex, and diagnosis. All of the treated patients were followed up for at least 5 years and some for as long as 8½ years. The maximum period of followup for the control group was 10 years. Of the treated group, 204 (44.6%) were paroled (102 received insulin, 91 Metrazol and 11 E.S.T.) as compared with 103 (35.6%) of the untreated control group. After a 5-year period, 79 (23.8%) in the control group, 56 (29.3%) in the insulin group, 63 (26%) in the Metrazol group, and 8 (33.3%) in the E.S.T. group were out of the hospital. Analysis of results by diagnostic groups indicated that insulin coma therapy is more effective than convulsive therapy in schizophrenia, particularly in the catatonic and paranoid types, and that E.S.T. is more effective than either insulin or Metrazol in the treatment of the affective psychoses and depressions.

25. HOLLISTER, LEO, AND FITZPATRICK, WALTER F., JR. Oral Metrazol in the psychoses associated with old age. *Journal of the American Geriatrics Society,* 1955, 3, 197–200. (March.)

Forty patients were selected for the study of the effects of oral Metrazol on senile psychoses. Half of the group received Metrazol and the other half a placebo tablet. No personnel other than the pharmacist knew which patients received active medication. Ten patients showed some improvement during the period of study; 5 had received Metrazol, and 5 placebos. The authors conclude from their findings that oral Metrazol is without value in the treatment of patients with senile psychoses.

26. HOLT, W. L., JR. Practical value of convulsive shock therapy research. *Diseases of the Nervous System,* 1947, 8, 112–117.

A group of schizophrenic patients treated with Metrazol therapy were matched with a similar untreated control group. Of 62 of the treated patients who were ill no longer than 1 year, 45% were recovered, 26% were much improved, and 19% were improved 1 year after treatment was started; a total of 74% were at home. Of 61 similar control patients, 26% were recovered, 16% were much improved, 35% were improved, and 51% were at home. In 32 of the treated cases the symptoms of dementia praecox had been present for more than 1 year but less than 3 years. Of these, 16% were recovered, 19% were much improved, and 31% were improved 1 year after the beginning of treatment; a total of 44% were at home. In the control cases, ill the same length of time, none were recovered, 9% were much improved, 46% were improved, and 72% were at home. Twenty-eight chronic cases of dementia praecox were treated with Metrazol. Of these, none recovered, 7% were much improved, 45% were improved, and 14% were at home. Among 32 similar chronic controls, 3% were recovered, 3% were much improved, 41% were improved, and 34% were at home. In terms of the intensity of the illness the treated acute cases showed a 71% decrease in average intensity and a 72% decrease in the number of symptoms. The control group of acute cases showed a 51% decrease in symptom intensity and a 50% decrease in the number of symptoms. The same figures for the sub-acute cases were 46% and 40% for the treated cases and 37% and 27% for the controls. In the chronic dementia praecox group, Metrazol treatment was followed by a 28% decrease in symptom intensity as compared with a 23% decrease shown by the controls. The author concludes from these findings that Metrazol treatment is of lasting benefit only in the acute and sub-acute cases of dementia praecox. In a group of 35 patients with other types of diagnoses, Metrazol treatment in the first year of illness resulted in 91% being out of the hospital a year later as compared with 74% for a control group.

27. KAPERNICK, JOHN S. Metrazol for central nervous system arteriosclerosis in aging patients. *Geriatrics,* 1957, 12, 703–708. (November.)

Metrazol was administered for a period ranging from 1 to 10 years to 687 geriatric patients, with a clinical diagnosis of cerebral arteriosclerosis, each of whom was observed for an average of 2½ years. The average dose used was 9 gr. daily. During the course of this study, 100 patients were selected to validate the observations on the "good response" group. Fifty patients previously judged "good response" were given a placebo tablet identical to the Metrazol tablet, and the other 50 patients were advised to discontinue their Metrazol and were given vitamin B and multivitamins as a substitution. After 60 days, 4 patients reported feeling greater improvement with vitamin therapy, or felt better on placebo medication. A total of 10% of the entire 100 patients did not voluntarily return for further medication with Metrazol and were classified as "failure responses." Of the 687 patients treated with Metrazol, 574 (83.5%) were assessed as showing good to excellent responses. The author hypothesizes that if the placebo test had been used on the entire group of 574 patients who responded well, perhaps an additional 10% would have been classed as failures altering the total responses graded good to excellent to approximately 75%. The author concludes that Metrazol appears to be a safe

and useful adjunct in the treatment of the arteriosclerotic patient.

28. KASS, IRVING, AND BROWN, EARL C. The use of Metrazol as a mood conditioning drug: a discussion as to its mode of action. A preliminary report. *Journal of Nervous and Mental Disease,* 1956, 123, 57–64. (January.)

Three geriatric patients with diagnoses of chronic brain syndrome were tested with subconvulsive doses of Metrazol while three similar control patients received placebos. During a second phase of the experiment the control patients were given Metrazol injections. In an effort to see if the clinical changes effected by Metrazol could be measured the following tests were administered: the Comprehension, Similarities and Picture Arrangement subtests of the Wechsler-Bellvue, the entire Wechsler Memory Scale, Year X through Adult I of the Porteus Mazes, and Cards II, IV, and VII of the Rorschach. At no time did the psychologist administering the tests have any awareness of the patient's clinical history nor did he know which ones were receiving Metrazol as opposed to placebos. From clinical observations the authors felt that Metrazol did tend to modify social behavior in arteriosclerotic patients. Psychometrically, measurable improvement was noted in orientation, in ability to size and comprehend a practical social situation, and in associate learning of new and unfamiliar material. However, from the same tests it was found that Metrazol had a detrimental effect on visuomotor functioning and on the mental control needed for prolonged attention and concentration.

29. KEPNER, RICHARD DEMONBRUN. Evaluation of Metrazol therapy of the psychoses. *Medical Record,* 1941, 154, 423–426; 428–433. (December 3.)

A detailed statistical analysis is presented of 152 psychotic patients treated with Metrazol convulsive therapy. Results in this group are compared with results in recent admissions not treated with Metrazol, and also with results in all admissions over a period of 11 years, having the same type of psychoses. An analysis of the data showed that only 5.3% of the Metrazol treated patients were discharged and 11.9% were paroled, as compared with 41.8% and 13.4% respectively of the first admissions who did not receive Metrazol. The author concludes that Metrazol therapy should be limited to cases which have remained inaccessible after other methods have been tried.

30. KINGSLEY, GEORGE R., AND FREED, HERBERT. Effects of insulin and Metrazol therapy on cerebrospinal fluid proteins. *Archives of Neurology and Psychiatry,* 1941, 45, 289–295. (February.)

Changes in cerebrospinal fluid protein were studied in a group of 14 schizophrenic patients receiving insulin treatment, in another group of 26 receiving Metrazol, and in an untreated control group of 10 patients. The immediate effect of Metrazol was a lowering of the albumin-globulin ratio. After 1 to 8 weeks of treatment and a rest of 3 to 4 days, the albumin and albumin-globulin ratio increased, while the globulin decreased. Insulin caused a rise in globulin and a depression of the albumin-globulin ratio. When the treatment was discontinued, the albumin-globulin ratio returned to higher values, while globulin decreased. No significant changes were found in the untreated control group.

31. KISKER, GEORGE W. A projective approach to personality patterns during insulin-shock and Metrazol-convulsive therapy. *Journal of Abnormal and Social Psychology,* 1942, 37, 120–124. (January.)

An investigation is presented on the use of the Rorschach form-perception technique as an objective measure of personality organization and change during the course of insulin- and Metrazol-shock therapy. Twenty-eight psychotic patients were examined immediately before therapy was initiated, and at approximately 1-month intervals throughout the course of treatment. Eleven normal control subjects were also given a Rorschach examination at monthly intervals. Detailed Rorschach summaries were made for all ex-

aminations. A considerable shift was found in the several Rorschach signs from one examination to another, both in the psychotic patients and in the control subjects, but was more striking in the psychotics. However, the response differences in the psychotic series were those which take place within the individual psychotic framework, rather than changes in the direction of a normal pattern. This trend was found to be less true for those patients who showed the most complete clinical recovery; however, even in these cases certain rigid elements of the psychotic pattern remained little affected by treatment. In the light of these findings, the author questions whether insulin or Metrazol therapy actually brings about any deep restructuralization of the personality pattern or of its underlying dynamics.

32. KOLOMEYER, NORTON. A clinical evaluation of mephentermine sulfate and pentylentetrazol as stimulant therapy for the geriatric patient. *Journal of the American Geriatrics Society,* 1958, 6, 415–423. (May.)

A group of 65 unselected, chronically ill geriatric patients were treated for 4 weeks with oral Metrazol and then for 4 weeks with oral mephentermine sulfate in an attempt to evaluate the effects of stimulant therapy. The effectiveness of the two drugs was found to be roughly comparable; fifteen patients (31%) exhibited definite improvement with Metrazol and 23 (42%) with mephentermine sulfate.

33. KWALWASSER, SIMON. Report on 441 cases treated with Metrazol. *Psychiatric Quarterly,* 1940, 14, 527–546. (July.)

The results obtained with Metrazol in 441 psychotic patients were found to be extremely poor when compared to those obtained by other authors with either insulin therapy or nonspecific therapy. Only 32 cases (7.2%) were "much improved" and 114 (25.9%) were "improved" at the end of treatment. From 5 months to 1 year later these figures dropped to 8 (1.8%) and 113 (25.6%). In comparison, statistics on nonspecific therapy have showed from 25% to 44% improvement. The author also notes that Metrazol therapy also has many inherent dangers, i.e., vertebral fractures were found in 29 of 100 patients x-rayed in addition to many other skeletal fractures and dislocations.

34. LAVERNE, ALBERT A. Narco-stimulation. *American Journal of Psychiatry,* 1959, 115, 738–740. (January.)

The author describes a new technique of Metrazol therapy in which the chemical action of a large dose of an analeptic upon the central nervous system is utilized without producing convulsions in any form and which avoids the anxiety that usually accompanies convulsive treatment. Eight of 16 schizophrenics (50%), 4 of 7 neurotics (57%), and 1 out of 2 (50%) behavior disorders showed sustained clinical improvement up to 6 months. Of 10 control patients (6 schizophrenics and 4 neurotics) treated only with anesthetic thiopental, only 2 (20%) improved. The method was found to have no significant side effects or contraindications.

35. LAVERNE, ALBERT A., AND PADULA, LOUIS J. Narco-stimulation. *Diseases of the Nervous System,* 1958, 19, 534–537. (December.)

The author describes a technique of Metrazol therapy called narco-stimulation in which first atropine, then thiopental, and then Metrazol are administered through the same needle. No convulsion is induced and there is little or no apparent anxiety. Of 50 experimental patients who were refractory to previous forms of treatment, 20 showed improvement. Of 20 control patients treated only with anesthetic thiopental, 5, or 20% improved. Narco-stimulation was found to have no significant side-effects or contraindications.

36. LEHOCZKY, T., ESZENYI, M., HORÁNYI-HECHST, B., AND BAK, R. Katamnestische Untersuchungen über die Insulin-Shock- und Konvulsionstherapie der Schizophrenie. (Followup investigation of insulin shock and convulsion therapy of schizophrenia.) *Zeit-*

schrift für die gesamte Neurologie und Psychiatrie, 1939, 166, 24–80.

The authors' findings are based on a study of 419 schizophrenic patients; 118 were treated with insulin, 61 with Metrazol, 22 with a combination of insulin and Metrazol, and 218 who received no active treatment. On followup the number of remissions in the treated acute cases (ill less than 6 months) was smaller than that for the untreated cases, i.e., 32.07% for insulin, 28.05% for Metrazol, and 46.5% for the controls. For the sub-acute cases (ill from 6 to 12 months), the remission rates were almost the same for all three groups, i.e., 30% for the insulin, 25% for the Metrazol, and 23% for the controls. The remission rates for the sub-chronic cases (ill from 1 to 2 years) were 41.6% for those treated with insulin, 14.3% for those treated with Metrazol, and 15.38% for the controls. In the chronic cases (ill longer than 2 years) there was no greater improvement in the insulin group than in the control group, i.e., 10%.

37. LEVY, NORMAN A., SEROTA, H. M., AND GRINKER, ROY R. Disturbances in brain function following convulsive shock therapy. *Archives of Neurology and Psychiatry,* 1942, 47, 1009–1029. (June.)

Twenty-three patients with various types of depression and schizophrenia were studied clinically and electroencephalographically. Eleven were treated with Metrazol induced convulsions and 12 with electrically induced convulsions. In the Metrazol series 4 patients recovered, and 1 improved, whereas in the electrically treated series 7 recovered and 2 improved. Impairment of intellectual function was found to occur much more frequently in the electrically treated patients (8 out of 13) than in the Metrazol treated patients (2 out of 11). Seven of the Metrazol treated patients and 5 of the electrically treated patients showed electroencephalographic evidences of cerebral disturbance. However, recovery from these disturbances occurred in most patients in a few weeks. In the more severely affected patients evidences of impaired function lasted as long as 6 months.

38. LEVY, SOL, AND SOUTHCOMBE, R. H. Value of convulsive therapy in juvenile schizophrenia. *A.M.A. Archives of Neurology and Psychiatry,* 1951, 65, 54–59.

This study reports the results of various shock treatments on 47 juvenile schizophrenics and compares them with those for a group of 56 similar patients who received no treatment other than institutional care and occupational therapy. Eleven had at least one full course of electric shock therapy and, except for one patient, a full course of insulin shock treatment. Seventeen had at least one course of Metrazol shock and 12 of these had an additional course of insulin. Nineteen received only insulin shock therapy. Good results in the treated group were achieved in only 6 of the 47 patients (12.6%) as compared with 9 (16%) in the untreated group. For 10 (21.5%) of the treated patients results were considered as fair to poor as compared with 12 (21.4%) in the untreated group. A further comparison with adult schizophrenics receiving shock therapies in the same hospital showed that approximately 31% responded favorably as compared with the 12.6% for the juvenile schizophrenics. The authors conclude from these findings that convulsion therapies do not appear to influence the course of schizophrenia in patients under 18 years of age.

39. LIEBERMAN, A. L., SCHWARTZ, S. S., AND COOPER, M. Evaluation of intravenous and oral use of Metrazol in hospitalized arteriosclerotic psychiatric patients. *Geriatrics,* 1954, 9, 371–374. (August.)

A series of 41 geriatric patients with chronic psychiatric disorders plus arteriosclerotic changes were used to evaluate the effects of intravenous and oral Metrazol. Seventeen patients were given the drug intravenously, 11 received the drug orally, and 13 received placebos. All were housed and treated on the same ward. An evaluation of the psychological tests administered before and after treatment failed to show any statis-

tically significant differences between the 3 groups. However, on the basis of clinical observation, one-third of the intravenous group, and about one-half of the oral group showed significant improvement, and about one-fourth of the placebo group showed changes suggesting improvement.

40. LINDEN, MAURICE E., COURTNEY, DOUGLAS, AND HOWLAND, ALLAN O. Interdisciplinary research in the use of oral pentylenetetrazol (Metrazol) in the emotional disorders of the aged. Studies in gerontologic human relations. V. *Journal of the American Geriatrics Society,* 1956, 4, 380–399. (March.)

The effects of Metrazol on the psychosis of the senium were studied using 30 institutionalized women whose average age was 76.6 years. The patients were divided into an experimental and a control group, the former receiving Metrazol plus vitamins, the latter vitamins alone. Eight researchers, a psychiatrist, a clinical psychologist, a research psychologist, a statistical analyst, a medical internist, an electroencephalographer, a laboratory pathologist, and a psychiatric nurse acted as observers; only the psychiatrist knew the identity of the experimental and control patients. No significant change was found statistically, but a definite trend toward clinical improvement was noted in the Metrazol treated group.

41. LIPSCHUTZ, L. S., CAVELL, R. W., LEISER, R., HINKO, E. N., AND RUSKIN, S. H. Evaluation of therapeutic factors in pharmacologic shock. *American Journal of Psychiatry,* 1939, 96, 347–360. (September.)

Seven of 20 (35%) chronic schizophrenics were benefited by insulin therapy to the point of social recovery or marked improvement, as compared with a 20% spontaneous remission rate in a control group of 30 patients. Coma was found to be essential for the production of improvement. Metrazol was only half as effective as insulin in chronic schizophrenics. Paranoid schizophrenics responded best to insulin; agitated catatonics to Metrazol.

42. LONG, R. H. Metrazol in the treatment of mental disease and a report on its use at the State hospital. *North Carolina Medical Journal,* 1940, 1, 184–187. (April.)

Of 91 unselected cases of schizophrenia treated with Metrazol, 18.7% had full remissions, 28.6% had social remissions, and 31.8% were improved. On comparing the duration of hospitalization for this group of treated cases with a similar group of untreated cases it was found that: (1) for treated cases, ill 6 months or less, the average hospitalization period was 3 months and 4 days as compared with 8 months and 23 days for untreated patients; (2) for the treated cases ill 6 months to 2 years before admission the average stay in the hospital was 6 months and 25 days as compared with 18 months and 17 days for untreated cases. The author concludes that although Metrazol is not a panacea for all mental ills, it is a distinct adjunct to psychiatric treatment and definitely shortens the period of hospitalization.

43. LOW, ABRAHAM A. The present status of the shock treatment of the "functional" psychoses. *Illinois Medical Journal,* 1939, 75, 169–173. (February.)

In a series of 54 schizophrenic patients treated with insulin shock therapy 37.5% full recoveries and 12.5% social recoveries were obtained for those who had been ill less than 6 months. The combined recovery rates for all cases (new and old), however, were no more than 24.1% full recoveries and 11.1% social recoveries. In another series of 69 schizophrenics treated with Metrazol a recovery rate of 40% was obtained in the acute cases (ill less than 6 months). The combined remission rates for both acute and chronic cases was 23.3% full recoveries and 8.7% social recoveries. In an attempt to increase the above recovery rates, combined shock treatment was given to 81 schizophrenic patients. A rotation scheme was used in which each patient first received insulin, then Metrazol, then pyrexia, and finally narcosis with sodium amytal, or a repetition of the Metrazol shock. At the end of the fourth stage of

treatment the full recovery rate for this group was 39.5% and the social recovery rate 19.9%. In comparison to the above, the remission rates for a group of 128 untreated schizophrenics was 17.2% full recoveries and 8.6% social recoveries. The author notes that shock therapy may also be beneficial for other psychiatric conditions. The average length of hospital stay for a group of untreated manic-depressives was found to be 148 days, as compared with 16 days for a similar group treated with shock therapy. Good results are also reported with alcoholics and psychoneurotics.

44. LOW, A. A., SONENTHAL, I. R., BLAUROCK, M. F., KAPLAN, MAURICE, AND SHERMAN, IRENE. Metrazol shock treatment of the "functional" psychoses. *Archives of Neurology and Psychiatry,* 1938, 39, 717–736. (April.)

Metrazol shock treatment in a series of 66 psychotic patients gave a relatively high rate of recovery for persons with manic-depressive conditions (81.9%) and those "without psychosis" (100%). For the schizophrenic group treatment yielded a relatively high rate of recovery (66.7%) only if given within 6 months after the onset of the disease. The total percentage of recoveries for all patients was 45.5%. In contrast, the remission rate for a year previous to the introduction of Metrazol treatment was 25%. In a further comparison of Metrazol with sodium amytal narcosis in the treatment of manic-depressive conditions it was found that the rate of recovery for the former was 84.2% as compared with only 43.8% for the latter. No correlation was found in the Metrazol treated cases between prognosis and "convulsive threshold."

45. MEAD, S., MEULLER, E. E., MASON, E. P., KHEIM, T., AND KOUNTZ, W. B. A study of the effects of oral administration of Metrazol ® in old individuals. *Journal of Gerontology,* 1953, 8, 472–476. (October.)

Twenty-five elderly patients who were functioning at a low level of memory and judgment were matched and divided into two groups one of which received oral Metrazol and the other a placebo. The following criteria were used for evaluation: (1) staff and physician evaluations, (2) the Kent E.G.Y. Scale, (3) the Wechsler Memory Scale, (4) the Self Concept Questionnaire, (5) a picture series, (6) the flicker fusion frequency test, and (7) a muscle elasticity test. No significant improvement of the drug group over the control group was found for any of the measures tested. The authors conclude that oral Metrazol is without value when administered to elderly persons for the purpose of improving their memory, orientation, general strength, or well-being.

46. MORRISON, BENJAMIN O. Panogen, a geriatric supplement in the treatment of the aged. *Journal of the Louisiana Medical Society,* 1960, 112, 309–314. (August.)

Sixty-eight geriatric patients, half of whom were tested with Panogen (Metrazol, estradiol, methyl testosterone, iron, lipotropes, and vitamins), and the other half with a placebo, were studied for 5½ months. Fifty-six percent of the patients treated with Panogen and 47% of the patients treated with placebo showed an overall improvement. The author concludes from his findings that more personalized attention for geriatric patients can measurably improve their physical, mental and social status.

47. NIELSEN, JUUL C., GESHELL, STANLEY W., AND COEN, ROBERT A. A review of pharmacologic shock therapy at the Hastings State Hospital. *Diseases of the Nervous System,* 1942, 3, 122–126. (April.)

A review of results is presented of the treatment of psychotic patients with all types of pharmacologic shock therapy, i.e., i.m. insulin, i.v. insulin, Metrazol, combined insulin and Metrazol, and picrotoxin. In addition, 100 schizophrenic patients who received pharmacologic shock therapy are compared with a control group of 100 who did not. An analysis of results showed that 45% of the patients treated with Metrazol, 38% treated with i.m. insulin, and 36% who received combined treatment were at home. The re-

sponse to treatment was found to be more favorable the shorter the duration of illness. The younger of the schizophrenic patients showed a more favorable response to treatment. For patients with other diagnoses there was no correlation found between age and response to treatment. The results with picrotoxin and i.v. insulin were uniformly poor; only 10% of the patients treated with the former and 6% treated with the latter were at home. A comparison of 100 schizophrenics treated with pharmacologic shock with 100 similar patients treated by routine hospital methods showed that shock therapy had no special advantages; 47% of the treated patients were at home, as were 45% of the controls.

48. NOTKIN, J., DENATALE, F. J., NILES, C. E., AND WITTMAN, G. Comparative study of Metrazol treatment and control observations of schizophrenia. *Archives of Neurology and Psychiatry,* 1940, 44, 568–577. (September.)

A group of 100 schizophrenic patients were treated with Metrazol and the results compared with those obtained in a control group of 71 patients. Seventy-eight percent of the treated group and 84.5% of the control group had been ill longer than 18 months. Results showed that 18% of the treated patients improved, as compared with 8.4% of the control group. Relapses occurred in 11.1% of the treated patients, and in 33.3% of the control patients. None of the treated or control patients recovered. A correlation of outcome of treatment with age showed that in both the treated and in the control groups the patients who improved were younger than those who did not. In the treated group of patients who improved the paranoid and the catatonic type were equally represented; in the control group the catatonic type predominated.

49. NOTKIN, J., WATTS, L. E., SHANNON, G. W., NILES, C. E., AND DENATALE, F. J. A comparative study of the combined Metrazol-hypoglycemic shock treatment and spontaneous improvements in schizophrenia. *Journal of Nervous and Mental Disease,* 1943, 97, 62–76. (January.)

This report is based on the results of combined insulin and Metrazol treatment of 100 schizophrenic patients (50 men and 50 women) and the result of observation of 50 similar patients (38 men and 12 women) who recovered or improved spontaneously while undergoing various tests in preparation for treatment. Various degrees of improvement took place in 37% of the treated patients, but none of them recovered, whereas in the spontaneously improved group there were recoveries ranging from 10% to 5% in proportion to duration of illness. Depending on the duration of psychosis the percentages of "markedly improved" and "improved" for the treated group ranged from 50% to 4.8% and from 66.7% to 24.1% as compared with from 75% to 30% and from 15% to 70% for the untreated group. Relapses occurred in 54.4% of the treated patients and in 16% of the patients showing spontaneous improvement. Remissions were longer lasting in those patients with a shorter duration of psychosis and were more enduring and of a better quality when they occurred spontaneously than when they were obtained by treatment.

50. O'CONNELL, J. J., AND PENROSE, L. S. Tests of psychomotor efficiency in patients treated with Metrazol. *Journal of Mental Science,* 1941, 87, 183–191. (April.)

Tests of reaction time, strength of grip and tapping rate were used to measure the effects of Metrazol therapy on motor efficiency in 15 male and 15 female patients. Tests were given throughout the course of treatment and the results compared with those obtained in 72 controls (30 normals and 42 untreated patients). Most treated patients showed reaction times significantly greater than normal at the first test and, after a few treatments, reactions of normal speed were consistently obtained. No similar improvement was found in the untreated control patients on retesting. These results, however, could not be considered conclusive due to the fact that few of the treated patients were sufficiently cooperative for useful comparisons

to be made. No statistically significant improvement could be demonstrated on the strength-of-grip test due to the amount of variation from day to day in the control group of patients. Cooperation on the tapping test was good, and records of the 30 treated patients were able to be compared with those of the controls. The correlation between degree of remission and the total change in tapping rate at the end of treatment was found to be $+0.38 \pm 0.17$. The authors attribute this improvement to a general easing of psychomotor activity brought about by the convulsions.

51. PACELLA, B. L., AND BARRERA, S. E. Followup study of a series of patients treated by electrically induced convulsions and by Metrazol convulsions. *American Journal of Psychiatry,* 1943, 99, 513–518. (January.)

The authors present a followup study of 126 patients (73 schizophrenics, 33 manic-depressives, 6 involutional psychotics and 17 psychoneurotics) treated by means of Metrazol convulsions, and 144 patients (68 schizophrenics, 39 manic-depressives, 14 involutional psychotics, and 23 psychoneurotics) treated by means of electrically induced convulsions. All cases were followed for periods exceeding 6 months subsequent to treatment. A statistical analysis of results indicated that the therapeutic effects of both methods were essentially the same, particularly in those cases diagnosed as psychotic. However, electric shock was found to be slightly more efficacious in terms of immediate results. The authors suggest that, in the light of these results and in consideration of the undesirable effects produced by Metrazol therapy, electric shock be used in preference to Metrazol when convulsive therapy is indicated.

52. PALMER, H. A. An experimental approach to the determination of comparative efficiency of insulin and convulsion therapy. *Journal of Neurology and Psychiatry,* 1942, 5, 10–13. (January–April.)

In an effort to compare the efficacy of individual therapies the author selected a group of 100 patients in a military mental hospital. Thirty were treated with Metrazol, 30 with insulin, 30 with electric shock, and 10 served as untreated controls. Results are expressed in terms of a "score" in which 10 marks were given for full recovery making a total possible score of 300 for each group. Scores for the three treated groups were 268 for Metrazol, 238 for insulin, and 247 for electric shock. In comparison, the score for the control group was only 31. The author notes that despite the nearly equal efficiency of Metrazol and insulin the former is slightly more efficient, very much cheaper, and easier to apply.

53. PENROSE, L. S., AND MARR, W. B. Results of shock therapy evaluated by estimating chances of patients remaining in hospital without such treatment. *Journal of Mental Science,* 1943, 89, 374–380. (July–October.)

A statistical method for evaluating shock therapy is presented by which the number of treated patients who remain in the hospital on any given date can be compared with an expected number based on a control group of cases matched according to sex, age on first admission, and lapse of time since first admission. Using this method, the authors present the results of shock treatment on 1,600 patients (1,333 treated with Metrazol, 196 with insulin, and 71 with both Metrazol and insulin). After 2 years 661 patients treated with Metrazol, 97 treated with insulin, and 49 treated with both were still in the hospital. In comparison, the number of patients expected to still be in the hospital, based on the control figures, were 842.2 for those treated with Metrazol, 105.8 for insulin, and 36.1 for those treated with both. There were, therefore, a total of 177.1 fewer patients on the hospital books than would have been expected if no shock treatment had been given. However, 1 year later this figure dropped to 107.1 which the authors attribute to a tendency for treated patients to return to the hospital after they have been discharged. On the whole, they calculate that 6% to 11% of those patients treated with

Metrazol or insulin stay out of the hospital 1 or more years.

54. POLLOCK, HORATIO M. A statistical study of 1,140 dementia praecox patients treated with Metrazol. *Psychiatric Quarterly,* 1939, 13, 558–573. (July.)

The author presents the results obtained with Metrazol therapy in 1,140 cases of dementia praecox treated in the New York civil State hospitals and compares them with those obtained in a group of patients treated with insulin, and those obtained in a control group who received no special drug treatment. In the Metrazol group 1.6% of the patients recovered, 9.9% were much improved, and 24.5% were improved. In comparison 12.9% of the insulin patients and 11.2% of the control group recovered, 27.1% in the insulin group and 7.4% in the control group were much improved, and 25.3% in the insulin group and 7.5% in the control group were improved. A comparison of the results between insulin and Metrazol according to the type of dementia praecox showed that insulin therapy was superior in each of the several types. Other statistical data are presented correlating the outcome of Metrazol treatment with the age of the patient at the beginning of treatment, with the duration of psychosis before treatment, and with the duration of treatment. A summary is also presented of the types of injuries sustained by 87 of the 1,140 treated patients.

55. POLÓNIO, PEDRO. L'insuline et l'insuline-Cardiazól dans les maladies mentales. (Insulin and insulin-Metrazol therapy in mental disease.) *Anais Portugueses de Psiquiatria,* 1951, 3, 87–89. (No. 3.)

An analysis is presented of 500 cases of psychosis treated with insulin plus Metrazol and compared with a control group of 500 untreated cases. Insulin treatment increased remissions in 24% of the dysplastic patients and in 30% of the leptosomes. However, in pyknics it increased remissions only by 2% and was completely ineffective in athletics. With insulin treatment the mean time in the hospital was reduced by one-third. The mortality rate over a 10-year period was 13% for the treated cases and 31.9% for the untreated controls.

56. RADICH, BRANKO. Metrazol treatment of the geriatric patient. *Postgraduate Medicine,* 1957, 22 (6), 603–608. (December.)

Over a period of a year, 109 geriatric patients with mental confusion due to senile cerebrovascular changes were treated with oral Metrazol. All patients initially received two tablets (200 mg.) of Metrazol four times a day—a total dosage of 800 mg. per day for a month. After this time the dosage was reduced to one-half the original amount and continued for an indefinite period. All patients were used as their own controls by substituting an identical placebo for the Metrazol tablet when the maximum benefit of the therapy had been attained. The placebo was given for a period of 3 weeks, with only the pharmacist and the physician in charge aware that there had been any change in medication. Seventy-four of the patients showed marked improvement, and 24 were moderately improved. When placebos were used in place of Metrazol, regression started within 2 or 3 weeks, but improvement was again noted when Metrazol treatment was resumed.

57. REESE, HANS H. Hypoglycemia and convulsive therapy in schizophrenia. Clinical observations and results. *Journal of the American Medical Association,* 1939, 112, 493–496. (February 11.)

Forty-seven schizophrenic patients were treated with insulin and the results compared with those obtained in the treatment of 37 similar patients with Metrazol. Thirteen (27.7%) of the insulin treated patients had full remissions, 5 (10.6%) had social remissions, and 7 (14.9%) showed improvement. In comparison 3 (8.1%) of the patients treated with Metrazol had full remissions, 1 (2.7%) had a social remission, and 8 (21.6%) showed improvement.

58. ROBERTS, CHARLES S. Followup report of 74 patients treated by pharmacologic shock

compared with matched controls. *Medical Bulletin of the Veterans Administration, Washington, D.C.*, 1942, 19, 49–59. (July.)

A 4 year followup study was done on 74 schizophrenic patients of whom 1 received Metrazol alone, 27 insulin alone, and 46 both insulin and Metrazol. The results of their treatment were compared with those of 74 untreated controls matched for age, diagnosis, sex, duration of psychosis, and race. At the end of the first followup period, 30–90 days after termination of treatment, 21.6% of the treated group showed some degree of improvement, as compared with 8.1% of the control group. At the close of the first year following termination of treatment, 19% of the treated group showed some degree of improvement, as compared with 6.8% of the control group. At the end of the second and third years the treated and control groups were almost equal in regard to improvement. In the fourth year, 8.3% of the treated patients showed some degree of improvement, as compared with 10% of the control group. Neither the acuteness of the illness nor the age of the patient had any effect on prognosis. The author concludes from these findings that pharmacological shock therapy facilitates improvement of a transient nature, but has no specific curative effect.

59. ROBINSON, DAVID B. Evaluation of certain drugs in geriatric patients. *A.M.A. Archives of General Psychiatry*, 1959, 1, 41–46. (July.)

Eighty female geriatric patients suffering from chronic brain syndrome were selected for study. Four matched groups were formed to receive chlorpromazine, reserpine, Metrazol, or a placebo. Results were evaluated by (1) a complete examination of mental status, (2) administration of the Fergus-Falls Behavior Rating Scale, and (3) psychometric testing, i.e., Parthington Pathway and Seguin Form Board. No statistically significant differences in beneficial effects were found between patients receiving active medication and those receiving placebos. A tendency toward a lower level of functioning was observed with each of the medications, as compared with spontaneous deterioration observed in the group given a placebo. This tendency was statistically significant in the patients who received chlorpromazine, but not for those who received reserpine or Metrazol. Undesirable side-effects (inertia, skin reactions, jaundice, and pallor) were most prevalent in the group treated with chlorpromazine. It is concluded that chlorpromazine, reserpine, and Metrazol are of little use in the treatment of senile patients found in State hospitals.

60. RODNICK, E. H. The effect of Metrazol shock upon habit systems. *Journal of Abnormal and Social Psychology*, 1942, 37, 560–565. (October.)

The author studied the effect of Metrazol shock upon habit systems by establishing a simple motor habit in a group of schizophrenics and then training them in a similar but incompatible habit wherein the first one had to be repressed. Twenty-one of the patients underwent Metrazol therapy and 21 served as untreated controls. Results showed that 14 of the Metrazol treated patients reverted to the older habit, that is, to the one learned first, as compared with 4 in the control group. These findings are believed to uphold the hypothesis that Metrazol weakens the more recently acquired habits to a greater extent than older habits so that the older habits again become dominant.

61. ROSS, J. R. The pharmacological shock treatment of schizophrenia. A statistical study of results in the New York State hospitals. *American Journal of Psychiatry*, 1939, 95, 769–779. (January.)

A survey is presented of the results of the insulin and Metrazol treatment of dementia praecox in all New York State hospitals and comparison is made with an untreated control group. Of 1,356 patients receiving insulin therapy 192 (14.2%) were reported as recovered, 280 (20.6%) as much improved and 357 (26.3%) as improved. A total of 523 patients were treated with Metrazol. Twenty-three (4.4%) of these re-

covered, 51 (9.8%) were much improved and 168 (32.1%) were improved. Of the control series of 1,039 untreated first admissions 36 (3.5%) recovered, 116 (11.2%) were much improved and 77 (7.4%) were improved. Statistics on the outcome of treatment according to duration of illness indicate that those patients who have been ill less than 6 months do best on insulin therapy (80.8% showed various degrees of improvement).

62. ROSS, JOHN R., AND MALZBERG, BENJAMIN. A review of the results of the pharmacological shock therapy and the Metrazol convulsive therapy in New York State. *American Journal of Psychiatry,* 1939, 96, 297–316. (September.)

In the N.Y. State Department of Mental Hygiene hospitals, 1,757 patients suffering from dementia praecox were treated with insulin and 1,140 with Metrazol. Recovery and improvement rates for the insulin-treated cases are significantly higher than those of the untreated control group. In the Metrazol-treated group there were fewer recovered cases than in the control group. A followup study done approximately 1 year after termination of treatment indicated that a significant portion of the insulin-treated patients tend to retain their improved state. An analysis of the data indicated that prognosis in insulin therapy is dependent largely on (1) the duration of illness, (2) the type of dementia praecox, and (3) the personality of the patient prior to illness.

63. SCHNACK, GEORGE F., SHAKOW, DAVID, AND LIVELY, MARY L. Studies in insulin and Metrazol therapy: II. Differential effects on some psychological functions. *Journal of Personality,* 1946, 14, 125–149.

The Stanford-Binet, the Kent-Rosanoff Word Association test, and an aspiration level test were administered to 70 male schizophrenic patients before and after treatment with insulin and Metrazol. The means of the test scores before and after treatment were compared and considerable change in the direction of improvement of mental functioning was noted in most of the measures. To test the significance of these changes comparison was made with individually matched untreated controls who had been given two tests while under routine hospital care. The results indicated that approximately two-thirds of the improvement in test scores could be attributed to the ordinary hospital regime and familiarity with the test situation. In general, patients with mental ages below 12 on the first test gained more than those with higher mental ages. Metrazol seemed to be more efficacious than insulin with the lower intelligence group and more deleterious with the higher intelligence group. Insulin, though helpful in both groups, seemed to be more effective in patients with higher intelligence.

64. SHEARD, M. H., COYNE, E., AND HAMMONS, P. A trial of oral pentamethylenetetrazol in senile patients. *Journal of Clinical and Experimental Psychopathology,* 1959, 20, 33–37. (January–March.)

Forty-four senile male patients, diagnosed as having a brain syndrome with senile deterioration or a chronic brain syndrome with cerebral arteriosclerosis, were randomly divided into two groups. One group received oral Metrazol and the other a placebo. Both groups were evaluated before and after treatment by a clinical interview, by a nursing staff evaluation, by a behavior rating scale, and by psychological tests (Comprehension subtest of the Wechsler Adult Intelligence Test, Wechsler Memory Scale, and Form Board of the Revised Minnesota Paper Form Board Test). No significant improvement was found in either the Metrazol or the control group. The authors conclude that Metrazol is of no value in the treatment of senile patients who show any definite degree of deterioration.

65. SHERMAN, IRENE, MERGENER, JOHN, AND LEVITIN, DAVID. The effects of convulsive treatment on memory. *American Journal of Psychiatry,* 1941, 98, 401–403. (November.)

Nine schizophrenics and one manic-depressive were treated by grand mal seizures induced electrically in four instances and with Metrazol and picrotoxin in six instances.

Four standard tests for immediate memory, one for recent memory and a "life situation" recent recall were administered before, during, and after treatment. An increase was found in the average scores of the four standard memory tests when the pre-treatment and post-treatment scores were compared. However, the increase was not found to be significant except in one test—"report of a paragraph heard." The authors conclude that grand mal seizures have no significant effect upon immediate or recent memory.

66. SKORODIN, B., FISHER, M. L., SCHLAN, L., MAURER, S., AND WILES, H. O. Meningeal permeability and Metrazol therapy. *Journal of Nervous and Mental Disease,* 1940, 92, 348–355. (September.)

A group of 53 patients treated with Metrazol and a group of 38 untreated controls were studied with the Walter bromide test. Each patient had 5 readings. In both groups a significant difference was found between readings one and two, while other differences were insignificant. The authors feel that the resemblance of the curve of the P.Q. in treated and untreated patients may be due to the effect of spinal damage on meningeal permeability.

67. SPIEGEL-ADOLF, MONA, AND FREED, HERBERT. Effects of Metrazol convulsions on the cerebrospinal fluid. *Confinia Neurologica,* 1939, 2, 228–237. (No. 4.)

Determinations were made of the non-electrolyte-electrolyte ratio by a combined conductivity and interferometry method on 101 samples of cerebrospinal fluid from 46 patients with schizophrenia before and after treatment with Metrazol. It was found that the ratio average was 0.26 for 35 untreated schizophrenics; for persons without organic diseases of the nervous system the ratio was 0.22, and for patients with organic diseases of the nervous system, exclusive of tumors of the brain and convulsive disorders, it was 0.30. After the first induced convulsion 60% of the patients, and after repeated convulsions, 82%, showed an increase in the ratio, with an average of 0.32. This corresponds to the average value for patients with epilepsy. The authors believe that this change in the ratio is the result of an increase of the tissue cleavage products in the cerebrospinal fluid, which in turn is secondary to changes in the cellular and vascular permeability.

68. STALKER, HARRY, MILLAR, MALCOM W., AND JACOBS, J. M. Remissions in schizophrenia. Insulin and convulsion therapies compared with ordinary treatment. *Lancet,* 1939, 1, 437–439. (February 25.)

The authors describe and compare the results obtained in the treatment of schizophrenia by ordinary hospital methods (investigation, understanding and discussion of the patient's personality, attempts at resocialization, occupational therapy, and attention to physical health), by hypoglycemia, and by treatment with convulsant drugs (Cardiazol and Triazol). Followup was done on the 129 patients who received ordinary hospital treatment for periods from 3 months to 5 years after discharge, and for the 48 patients who received insulin for from 3 to 9 months; no followup was done on the 41 patients who were treated with convulsant drugs. In the group which received ordinary hospital treatment 12% had complete remissions, 8% had social remissions, and 9% were at home improved. In the insulin group 13% had complete remissions, and 13% had social remissions, and 10% were at home improved. In the group treated with convulsant drugs, 10% had complete remissions, 0% had social remissions, and 32% were at home improved. Hypoglycemia was found to be most effective in the paranoid subgroup and in cases in which the affect was well preserved, whereas convulsion therapy seemed to be best suited for stupor reactions.

69. STEINBERG, D. LOUIS, AND HEILBRUNN, GERT. Evaluation of the newer treatments of dementia praecox. *Elgin State Hospital Papers,* 1941, 4, 46–53. (April); also in *Illinois Medical Journal,* 1939, 75, 405–410.

In comparing the results achieved with insulin and Metrazol therapy of schizophrenic

patients, it was found that insulin had a definite superiority as far as complete remissions were concerned, while there were more social remissions with Metrazol. A total of 120 cases were treated with insulin. Seventy-two of these were ill not over 18 months; of these 48 (67%) recovered, and 7 (10%) had social remissions. In the more chronic group (ill from 19 months to 5 years) there were 48 patients; only 1 (2%) recovered, and 7 (14%) had social remissions. A total of 300 patients were treated with Metrazol. Sixty-five of these were ill less than 18 months; of these, 18 (27%) recovered and 13 (20%) had social remissions. Of 146 cases, ill from 19 months to 5 years, 11 (7.6%) recovered and 6 (4.1%) had social remissions. For 89 patients, ill more than 5 years, no remissions at all were obtained. No correlation was found between the type of dementia praecox and the type of treatment used.

70. STEINBERG, D. LOUIS, AND NIERENBERG, H. H. The treatment of manic-depressive and involutional psychoses with Metrazol (pentamethylenetetrazol). *Elgin State Hospital Papers,* 1939, 3, 39–44. (January.)

Metrazol shock therapy was administered to a group of 50 patients suffering from manic-depressive psychosis. Of these 19 (38%) recovered, and 17 (34%) were improved in varying degrees. Of twenty-six patients in the manic phase 8 (30.8%) recovered, and 7 (26.9%) showed varying degrees of improvement. In comparison, the recovery rate for a control group of 27 manics was 81.5%, or twice that obtained in the treated group. Of 16 treated patients who were in the depressed phase, 7 (43.7%) made a complete recovery, and 7 (43.7%) showed varying degrees of improvement. The control group of depressed cases consisted of 15 patients, of whom 12 (80%) were discharged as recovered. The authors conclude from their findings that Metrazol therapy is not indicated as a routine procedure in the manic phase, but that it does have a place in the depressive and mixed phases of manic-depressive psychosis, as well as in the involutional psychoses.

71. STENBERG, SVEN. Den statistika metodiken för terapiförsök vid psykoser. I. Cardiazolbehandling med och utan konvulsioner. (Statistical method for evaluation of therapeutic results in psychoses. Cardiazol treatment with and without convulsions.) *Nordisk Medicin (Hygiea),* 1939, 4, 3278–3280. (November 4.)

The author reports the result of Metrazol therapy in 2 matched groups of schizophrenic patients. Ten of the patients received convulsive doses of Metrazol and 10 subconvulsive doses. Five of the patients who received convulsive doses of Metrazol showed improvement lasting for a half year, whereas only two treated with subconvulsive doses showed similar improvement.

72. SWENSON, WENDELL M., ANDERSON, DON E., AND GRIMES, B. P. A re-evaluation of the oral use of Metrazol in senile patients. *Journal of Gerontology,* 1957, 12, 401–403. (October.)

Twenty-eight female geriatric patients with psychiatric disorders were given two 1½ gm. tablets t.i.d. of oral Metrazol for 30 days and then three 1½ gm. tablets t.i.d. for a second period of 30 days. Twenty-six similar patients served as a control group and received an identical placebo tablet in the same dosage. Two independent raters evaluated both groups using the Ferguson Hospital Adjustment Scale at the beginning of treatment, at the period of increased dosage, and at the termination of treatment. No statistically significant differences were found between the two groups. The authors conclude from these findings that Metrazol, in the dosage used, does not objectively change the behavior of geriatric patients suffering from chronic brain syndrome with cerebral arteriosclerosis or from chronic brain syndrome with senile psychosis.

73. SWENSON, WENDELL M., AND GRIMES, BURTON P. Oral use of Metrazol in senile

patients. *Geriatrics,* 1953, 8, 99–101. (February.)

Twenty-five male patients with senile psychoses of various types were given Metrazol in oral capsules of 0.1 grams three times a day for 30 days. An equivalent control group received 0.1 gram capsules of sodium bicarbonate three times a day for the same period. All patients were evaluated simultaneously by three independent raters using the Elgin State Hospital Behavior Rating Scale prior to the administration of the drug and just after the 30 day course of treatment. An analysis of the data showed no significant differences between experimental and control groups, although, clinically, some of the patients receiving Metrazol were observed to be improved.

74. VELA DEL CAMPO, L., AND DE LA VEGA GUTIERREZ, P. Remisiones espontáneas y remisiones provocadas de la esquizofrenia. (Spontaneous and provoked remissions in schizophrenia.) *Medicina,* 1941, 9, 68–73. (July.)

Of 250 schizophrenic patients, admitted during the pre-shock era, 75 (29%) were able to leave the hospital. In comparison, the remission rate obtained with Metrazol was 32%, and that with insulin 62%.

75. WEIL, ARTHUR, AND LIEBERT, ERICH. A neuropathologic study of six cases of psychoses treated with Metrazol. *Elgin State Hospital Papers,* 1941, 4, 116–125. (April.)

The brains of six patients with dementia praecox, manic-depressive psychosis and involutional melancholia who were treated with Metrazol and those of two patients who were not were studied and compared. In comparison to the untreated patients the Metrazol cases showed a marked hypertrophy and hyperplasia of astrocytes, and, to a lesser degree, of microglia. Ganglion cell disease was less pronounced, although in one case there was a generalized severe disease of the neurons with neuronophagia. The authors note that these findings are very similar to those reported in rabbits following experimental injections of Metrazol.

76. WEINBERG, J., GOLDSTEIN, H. H., AND EDLIN, J. V. Chemotherapeutic and spontaneous recoveries from psychoses. A comparison as to quality. *Illinois Medical Journal,* 1940, 77, 266–268. (March.)

The authors have compared the type of recovery made by 24 patients treated with either insulin or Metrazol with that made by 24 patients who remitted spontaneously. The average residence in the hospital of patients who spontaneously remitted was 439.5 days as compared with 163.9 days for the chemotherapy recoveries. Superficially it seemed that there was no difference between a spontaneous recovery and one due to chemotherapy. However, the authors found a vast difference in the attitudes of the two groups toward their illness and toward the hospital which may have prognostic significance. The chemotherapy group tended to feel that their illness was treatable and that the hospital was a place to get well, whereas the spontaneous remission group felt they had to fight their own battle against terrific odds and worried about another attack placing them in a state institution for life.

77. WILLIAMS, GUY H., WILLIAMS, GUY H., JR., KINGSBURY, HELEN M., AND BIXBY, DAVID E. Experiences with the pharmacological shock treatment of schizophrenia. *American Journal of Psychiatry,* 1939, 95, 811–813.

The authors found that only 5.18% of all schizophrenics in the Cleveland State Hospital were discharged as improved over a 10 year period. These patients received routine hospital care, some psychotherapy, occupational therapy, and in some instances endocrine treatment. In comparison, 29.3% of 75 schizophrenics treated with Metrazol were found to be improved, and 25.3% were slightly improved.

78. WITTMAN, MARY PHYLLIS, AND RUSSELL, JAMES T. Mental efficiency levels before and after shock therapy. *Elgin State Hospital Papers,* 1941, 4, 70–81. (April.)

A test battery, consisting of seven tests of mental efficiency (personal information, general information, memory paragraph,

digits reversed, paired associates, orientation, and retention of memory paragraph), a check list of attitudes, and a rating scale of test reactions, was administered, before and after therapy, to 294 patients treated with Metrazol, 113 treated with insulin, and 89 treated alternately with insulin and Metrazol. Forty-two nonpsychotic subjects were used as controls. A general and marked improvement was noted following treatment with both insulin and Metrazol, but neither group reached the average levels of the control group. In the total Metrazol group, 81% of the patients showed improvement on the psychological test results immediately following therapy, and 71% were classified as improved on psychiatric evaluation. A year after termination of therapy 112 of these patients were rechecked with an equated battery of tests and 63% were found to still be functioning at a higher level of mental efficiency than they were before they received treatment. Of the total insulin group, 85% showed improvement in test results immediately following treatment, and 80% were considered improved on psychiatric evaluation. Fifty-four percent of the 42 patients rechecked 1 year later still showed improvement. The mixed therapy group showed a much smaller percentage of improvement than either the insulin or the Metrazol group. A direct correlation was found between improvement in mental efficiency levels and changes in the patient's attitudes. No evidence was found to indicate that memory defects occur following shock therapy.

79. WYLLIE, ANDREW M. Convulsion therapy of the psychoses. *Journal of Mental Science,* 1940, 86, 248–259. (March.)

The results of convulsion therapy in 144 psychotic patients are reported. Of these, 111 were treated with Metrazol, 9 with Metrazol followed by Triazol, and 24 with Triazol alone. A comparison between the two types of treatment showed that of the 111 cases treated with Metrazol alone only 25 (22.5%) recovered as compared with 10 (41.7%) of the 24 cases treated with Triazol alone. Relapse rates for the two groups were 29% and 17% respectively. The author concludes from these findings that Triazol is more effective than Metrazol in producing stable remissions. The mortality rate with convulsion therapy was found to be 0.54%. Complications encountered were various fractures and dislocations, especially of the neck of the femur, the activation of latent pulmonary tuberculosis, prolonged amnesia, and prolonged rise in blood pressure.

80. ZISKIND, EUGENE, LOKEN, ROBERT, AND GENGERELLI, J. A. Effect of Metrazol on recent learning. *Proceedings of the Society for Experimental Biology and Medicine,* 1940, 43, 64–65. (January.)

Six patients (2 chronic encephalitics, 1 manic-depressive, 1 involutional melancholic and 2 schizophrenics) and 6 controls (4 normals, 1 chronic encephalitic, and 1 recovered manic-depressive) were used to study the effects of Metrazol on recent learning. A code transcription technique was used in which the patient was asked to transcribe from memory a nonsense syllable code into appropriate blank spaces as rapidly as possible. The subject worked 4 minutes, rested 2 minutes, was given 6 minutes of practice at transcription, rested another 2 minutes, and then was given a 4-minute retest. During the following week 2 or 3 Metrazol injections were administered, and at the end of the week another 4-minute retest was given. As one control procedure the same patients were given an alternate and comparable form of the code transcription test, but during the period of forgetting no Metrazol injections were given. The same tests were also given to the controls who received no Metrazol at all. The data showed that performance after Metrazol injections resulted in a score of 27.8% lower than when the same patients were not given Metrazol. The six control subjects showed no loss at all, but a small mean gain of 3.5%. The authors conclude from these findings that the impairment in learning in Metrazol therapy is due to impaired memory.

81. ZISKIND, EUGENE, SOMERFELD-ZISKIND, ESTHER, AND ZISKIND, LOUIS. Convulsive therapy (Metrazol) in the affective psychoses. A controlled series covering a three-year period. *Bulletin of the Los Angeles Neurological Society,* 1943, 8, 43–52. (June.)

The authors compare the results obtained with 59 cases of affective psychoses treated with Metrazol with those obtained in a control group of 74 similar untreated cases. Followup ranged from 4 to 40 months with an average of 22 months. Partial and full remissions together were 89% in the treated and 72% in the control cases. There were 9 deaths in the untreated cases (6 from suicide and 3 from exhaustion) and 1 suicide in the treated cases. Recurrences of illness occurred twice as frequently in the controls as in the treated series, i.e., 12% and 6% respectively. Of the patients 60 years of age and over only 29% who were treated had remissions, as compared with 38% in the control group.

82. ZISKIND, EUGENE, SOMERFELD-ZISKIND, ESTHER, AND ZISKIND, LOUIS. Metrazol and electric convulsive therapy of the affective psychoses. *Archives of Neurology and Psychiatry,* 1945, 53, 212–217. (March.)

The authors compare the results obtained with treated and untreated patients with affective psychoses seen in private practice over a 5 year period. Followup period ranged from 6 to 69 months, with an average of 40 months. Of the 88 treated patients, 58 received Metrazol and 30 electric shock therapy. The untreated control group included 109 patients, of whom 43 had refused convulsive therapy, 50 had symptoms which were too mild to warrant this treatment, and 16 had physical diseases which contraindicated use of the convulsive method. For the 88 treated patients the immediate results showed 78% to be in full remission and 18% to be improved. On followup 90% of the treated patients were in full remission, as compared with 75% of the untreated controls. In the series of untreated patients there were 9 deaths from suicide and 4 from exhaustion, as compared with 1 death from suicide in the treated series. The incidences of ultimate full remission for those patients with the longest period of followup observation were essentially the same (88% and 86%) for treated and untreated patients respectively. Recurrences of illness occurred with equal frequency in both the control and treated series, the percentage being 21 and 18 respectively.

83. ZISKIND, EUGENE, SOMERFELD-ZISKIND, ESTHER, AND ZISKIND, LOUIS. Metrazol therapy in the affective psychoses. Study of a controlled series of cases. *Journal of Nervous and Mental Disease,* 1942, 95, 460–473. (April.)

The authors compare the results obtained with Metrazol therapy in 38 cases of affective psychoses with those obtained in 47 untreated control cases. There were 82% full remissions in the treated as compared with 38% in the untreated cases. Both complete and partial remissions were 92% in the former and 72% in the latter. Subsequent to examination the average duration of illness was 1½ months with treatment and 6 months without treatment. Five of the control cases died (3 from suicide and 2 from exhaustion) and one of the treated cases (from suicide). Sub-convulsive doses of Metrazol were found to predispose to therapeutic failure. The following complications of treatment are reported: (1) clinical fracture (6%); (2) subclinical fractures of the spine (31%); (3) transient memory impairment (56%); and (4) transient cardiac arrhythmia (3%).

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